Respiratory Syncytial Virus-Associated Lower Respiratory Tract Infection in Under-5-Year-Old Children in a Rural Community of Central Thailand, a Population-Based Study

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Abstract

The population-based cohort study on the epidemiology of respiratory syncytial virus (RSV)-associated lower respiratory tract infection (LRI) (RSV-LRI) was conducted in Takhli district from November 1998 to February 2001. The incidence of RSV-LRI was 12.6/1,000 child-year and 5.8/1,000 child-year during the first and second year, respectively. RSV accounted for 35.8 per cent of all LRI cases during the first year and significantly decreased to 17.5 per cent during the second year. Three-quarters of RSV-LRI occurred among children under 2 years old (76.6% during the first year and 62.2% during the second year). Most of RSV-LRI in both years occurred from July to October. Risk factor for morbidity of RSV infections were age less than or equal to 2 years (OR = 2.38, 95% CI = 1.22-4.67 p = 0.009) and sleeping with more than 3 persons in the patient's bedroom (OR = 2.92, 95% CI = 1.42-6.00, p = 0.002). Most RSV-LRI (63.9%) were clinically diagnosed as having pneumonia. No RSV-LRI deaths were detected. During the first year, RSV subtype B was predominate, in contrast to the second year when subtype A was more predominate. Further research to determine the annual change in subtype of RSV-LRI and correlation of severity of disease with specific subtypes needs to conducted in order to prepare for the future introduction of a vaccine.

Key word : Respiratory Syncytial Virus, Lower Respiratory Tract Infection

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In Thailand, acute respiratory tract infection (ARI) accounts for approximately 25 per cent of deaths and the mortality rate for pneumonia is ranked among the top 5 causes of death in children under one year of age[1]. Respiratory syncytial virus (RSV) is the main viral pathogen responsible for acute lower respiratory tract infection (LRI) in both developed and developing countries. In Thailand, hospital-based data showed that RSV accounted for 39.8 per cent of viral ARI (both LRI and upper respiratory tract infection)[2,3]. A previous hospital-based study in Thailand among 399 children with LRI during 1989-1991 revealed only common age group and variation of subgroups during the study period[4]. Little is known about the magnitude of RSV-associated LRI (RSV-LRI) especially data from population-based studies in Thailand. Furthermore, the data on the common age group, characteristics of targeted children and seasonality are still unknown in this setting. Since this information is very important for further development of prevention and control measures of RSV infection in Thailand, the authors, therefore, conducted the present study.

OBJECTIVES

General

To study the epidemiology RSV-LRI among under-5-year-old children from a rural community in central Thailand.

Specific

1. To examine the age-specific incidence rate of RSV-LRI.
2. To identify the risk factors and study the natural history of RSV-LRI.
3. To examine the seasonality of RSV-LRI and the subtypes of RSV responsible.

METHOD

Takhli district, Nakhon Sawan province, located in the central part of Thailand was selected as the area for this study for several reasons : the population under surveillance was large enough to generate about 58 births each month in which episodes of RSV-LRI could be identified during the 2-year period of study, there was a stable population, with one well-utilized primary source of medical care, good access to and utilization of the hospital which had well-equipped laboratory and medical utilities for collecting the specimens and treatment of sick children. There was a good transportation system to facilitate specimen processing.

At the beginning of the study, every under-5-year-old children in the community was recorded in a baseline census and provided with a unique identification number to ensure the correct calculation of incidence in the case of multiple episodes of RSV. There were 6,244 under-5-year-old children registered and followed for episodes of RSV.

A cohort population-based study design was used. All children under 5 years old in the study area as well as neonates were registered and followed for the period of 2 years and 4 months (from November 1998 to February 2001). When there was a new case of LRI, the subdistrict health workers were informed to refer the child to the district hospital where the study was being conducted.

The diagnosis and management of LRI were performed by the district physician using WHO standard protocol. Case report forms were filled up and nasopharyngeal specimens were obtained by direct aspiration and sent for further viral identification with subtyping at Siriraj Hospital in Bangkok by immunofluorescence staining. A chest X-ray was taken and interpreted to confirm the diagnosis of LRI. All staff involved (subdistrict health workers, pediatricians and nurses who collected nasopharyngeal specimens) and the processing method in the central laboratory by local laboratory technicians were screened to ensure appropriate standards.

Supervision of children was regularly carried out for active surveillance of LRI and identification of births, deaths and migrations, with modification of the denominator accordingly.

Statistics

Most of the data analysis used descriptive statistics (number, percentage) by SPSS software. The analytic statistics of univariate analysis (odds ratio, 95% confidence interval and p-value) was also used to determine the difference of risk factors between RSV-LRI and non-RSV LRI groups. In addition, spreadsheet software was used to determine person-time figures.

RESULTS

At the beginning, there were 6,244 under-5-year-old children registered. All were under the surveillance for an episode of LRI.

During the eigthteen-months study period, 7,890 children under 5 years of age were enrolled from November 1, 1998 to February, 2001. There were 215 and 257 episodes of new LRI during the first and second year of study, respectively; of which the number of RSV identified as the cause of LRI were 77 and 45, respectively. The number of LRI and RSV-LRI and the incidence of LRI and RSV-LRI during the first and second year are shown in Table 1.

Most of RSV-LRI occurred among children under 2 years of age in both the first year (76.6%) and second year of the study (62.2%). Overall, the proportion of RSV as a cause of LRI was 72.2 per cent as shown in Table 2. Recurrent episodes of RSV-LRI in the second year were found in three cases. Most of RSV-LRI occurred during the rainy season (July to October) in both studied years which was the same as the pattern of LRI as shown in Fig. 1.

The clinical diagnosis of RSV-LRI according to WHO guidelines revealed that more than 60 per cent of the cases in both studied years were diagnosed as having pneumonia, whereas, only 2.5 per cent were diagnosed with acute bronchiolitis and no cases were diagnosed as having croup as shown in Table 3. No death due to LRI was reported.

Risk factors of RSV-LRI cases were also compared between RSV-LRI and those LRI with RSV negative in the number of variables such as their own characteristics of the sick children and caretakers, crowding in households, indoor pollution etc. The results revealed that only 2 factors were significantly different between the 2 groups which were aged less than or equal to 2 years (the result in the first year) and sharing the same bedroom with more than 3 people (the result in the second year) as shown in Table 4 and 5.

Among RSV found in this study, subtype B predominated during the first year, whereas, subtype A predominated in the second year as shown in Fig. 2 and 3. During the study period, there were 8 cases of RSV-LRI whose subtypes could not be identified.

DISCUSSION

The incidence of RSV-LRI in this study was quite low when compared to a previous study conducted by Berman et al (1983) among under 5-year-old children (n=4,958) in an urban area of Cali, Colombia which was found to be 36/1,000 child-

Table 1. The number of LRI, RSV-LRI and the incidence of LRI, RSV-LRI during the first and second studied year.

Categories	First year	Second year
Number of LRI	215	257
Number of RSV-LRI	77	45
Incidence of LRI	35.6:1,000 child-years	31.2:1,000 child-years
Incidence of RSV-LRI	12.6/1,000 child-years	5.8/1,000 child-years

Table 2. Age distribution of children with RSV-LRI during the first and second studied year.

Age group (months)	First year		Second year		Total	
	Number	%	Number	%	Number	%
0-6	11	14.3	7	15.6	18	14.8
7-12	20	25.9	10	22.2	30	24.6
13-24	28	36.4	11	24.4	39	31.9
25-36	7	0.1	5	11.1	12	9.8
37-48	8	0.1	10	22.2	18	14.8
49-59	3	0.04	2	4.4	5	4.1
Total	77		45		122	

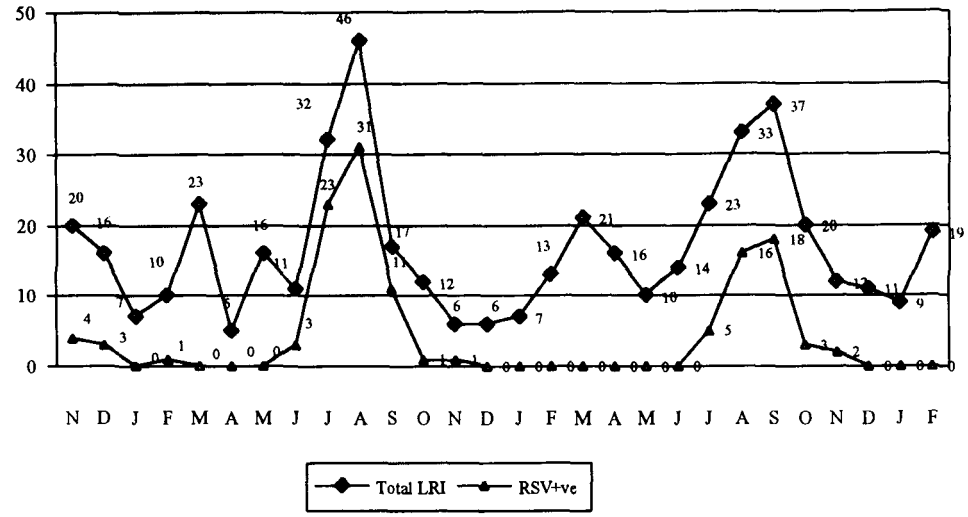

Fig 1. Number of patients with LRI and RSV-LRI, by month, during the study period.

Table 3. WHO clinical classification of patients with RSV- LRI.

Clinical diagnosis	First		Second		Total	
	Number	%	Number	%	Number	%
Pneumonia	50	64.9	28	62.2	78	63.9
Bronchitis	24	31.2	17	37.8	41	33.6
Acute bronchiolitis	3	3.9	0	0.0	3	2.5
Total	77		45		122	

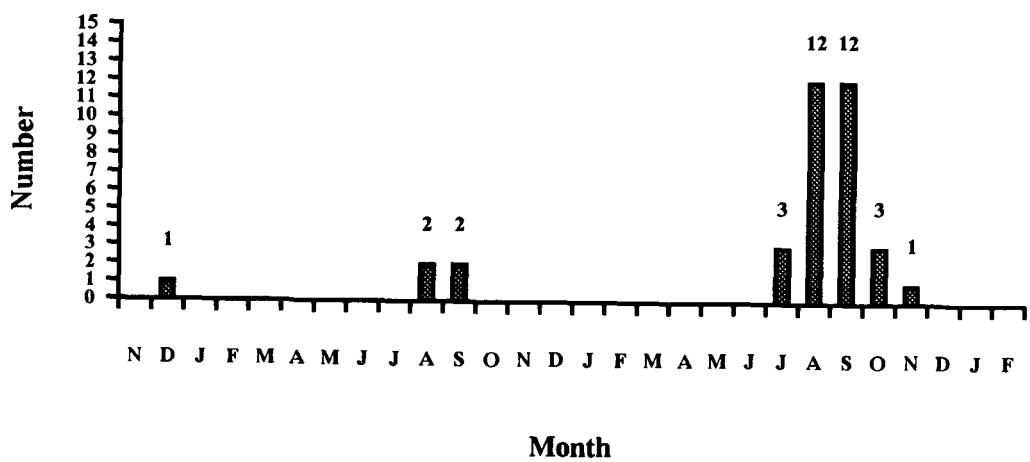

Fig. 2. Distribution of RSV subtype A by month during the study period.

Table 4. Risk factors related to RSV-LRI in the first year.

Variables	Groups	RSV+ve (N=77)		RSV-ve (N=138)		OR	95%CI	P
		n	%	n	%			
1. Sex	Male	47	61	73	52.9	1.39	0.76-2.56	0.312
2. Age (yr)	≤2	59	76.6	80	58.0	2.38	1.22-4.67	0.009*
3. Birth weight (g)	≤2,500	7	9.1	20	14.5	0.59	0.21-1.57	0.351
4. Exclusive breast feeding (mo)	≤4	35	45.4	78	56.5	0.64	0.35-1.17	0.15
5. No. of living brothers and sisters	>2	11	14.3	21	15.2	0.93	0.39-2.18	0.853
6. No. of family members in the household	>5	32	41.6	55	39.9	1.07	0.59-1.97	0.949
7. No. of persons sleeping in the patient's bedroom	>3	65	84.4	112	81.2	1.26	0.56-2.85	0.679
8. Smokers in the family	>2	14	18.2	27	19.6	0.91	0.42-1.97	0.946
9. Smokers in the house	>2	14	18.2	24	17.4	1.06	0.48-2.31	0.967
10. No. of cigarettes smoked per day	>10	25	32.5	47	34.1	0.93	0.49-1.75	0.931
11. Family member with chronic cough >3 weeks	>1	3	3.9	9	6.5	0.58	0.12-2.44	0.544
12. Use of charcoal or wood for cooking	Yes	36	46.8	65	47.1	0.99	0.54-1.79	0.925
13. No. of hairy animals	>20	11	17.9	22	18.1	1.04	0.45-2.41	0.923
14. Income/year								
Father	≤80,000	62	87.3	104	87.4	0.99	0.38-2.63	0.832
Mother	≤80,000	70	97.2	120	94.5	2.04	0.37-14.65	0.492

* = significant at 0.05 level

Table 5. Risk factors related to RSV-LRI in the second year.

Variables	Groups	RSV+ve (N=45)		RSV-ve (N=208)		OR	95%CI	P
		n	%	n	%			
1. Sex	Male	23	51.1	81	38.9	1.64	0.82-3.29	0.181
2. Age (yr)	≤2	28	62.2	144	69.2	0.73	0.36-1.51	0.460
3. Birth weight.	≤2,500	5	11.1	21	10.1	1.11	0.34-3.37	0.790
4. Exclusive breast feeding (mo)	≤4	23	51.1	104	50.0	1.05	0.52-2.09	0.976
5. No. of living brothers and sisters	>2	8	17.8	45	21.6	0.73	0.31-1.91	0.708
6. No. of family members in the household	>5	15	33.3	80	38.5	0.80	0.38-1.66	0.635
7. No. of persons sleeping in the patient's bedroom	>3	21	46.7	48	23.1	2.92	1.42-6.00	0.002*
8. No. of smokers in the family	>2	1	2.2	10	4.81	0.45	0.02-3.56	0.694
9. No. of smokers in the house	>2	2	4.4	10	4.81	0.92	0.0-4.72	1.000
10. No. of cigarettes smoked per day	>10/day	11	24.4	60	28.8	0.80	0.35-1.77	0.679
11. No. of family members with chronic cough >3 weeks	>1	0	0.0	0	0.0			
12. Use of charcoal or wood for cooking	Yes	14	31.1	89	42.8	0.60	0.29-1.26	0.201
13. No. of hairy animals	>20	10	22.2	26	12.5	2.00	0.82-4.82	0.145
14. Income/year (Baht)								
Father	≤80,000	43	95.6	183	88.0	2.94	0.64-18.67	0.184
Mother	≤80,000	43	95.6	202	97.1	0.64	0.11-4.75	0.635

* = significant at 0.05 level

Remarks: During the second year, there were 212 episodes of LRI occurred among 208 cases with RSV negative.

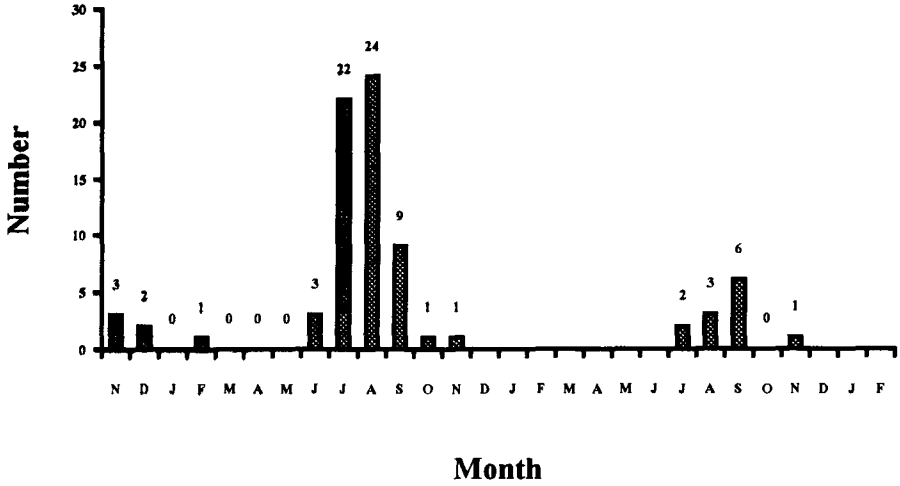

Fig. 3. Distribution of RSV subtype B by month during the study period.

year[5]. This was probably due to the low incidence of LRI itself. Even though the common age group found in this study was below 2 years of age, the proportion of age group below 6 months was quite low (15.1%) when compared to the other report (39%)[6]. Seasonality of RSV infection in this study was the same as other tropical countries.

The risk factors for RSV-LRI morbidity in this study were limited to only 2 factors as mentioned above, which were less than in the other study [7]. This was probably due to a wide range of the age group analysed and good achievement of nutritional and maternal child health programs in the area of this study. Variation of subtypes of the virus revealed in this study was the same as the previous hospital-based study in Thailand[4]. The fact that no death was reported in this study was problably due to several possible reasons ; virulent nature of the virus itself, early and appropriate treatment given to sick children and no severe risk factors such as cardiac disease, prematurity and pulmonary disease found among RSV-LRI children.

Further research to determine the annual change in subtype of RSV-LRI and correlation between severity of disease and subtype needs to be conducted in more rural communities in order to confirm the findings.

In addtion, in order to address more specific risk factors, the factors of interest which are supposed to be related with RSV disease should be conducted separately with a bigger sample size and focussing only on one specific age-group.

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REFERENCES

1. Sunakorn P, Chunchit L, Nilawat S, Wangwerawong M. Jacobs RF. Epidemiology of acute respiratory infection in children from Thailand. Pediatr Infect Dis J 1990; 9: 873-7.
2. Suwanjutha S, Chantarojanasiri T, Watthana-kasetr S, et al. A study of nonbacterial agents of acute lower respiratory tract infection in Thai Children. Rev Infect Dis 1990; 12 (Suppl 8): S923-8.
3. Puthavathana P, Wasi C, Kositanont U, Suwanjutha S, et al. A hospital-based study of acute viral infection of the respiratory tract in Thai children, with emphasis on laboratory diagnosis. Rev Infect Dis 1990: 12 (Suppl 8): S988-94.
4. Puthavathana P, Habanananda S, Raksakait K, et al. Respiratory syncytial virus; incidence by age, sex and seasonality, and subgroup prevalence during 1989-1991, Bangkok, Thailand. Southeast Asian J Trop Med Public Health 1995; 26: 514-20.
5. Berman S, Duenas A, Bedoya A, et al. Acute lower respiratory tract illness in Cali, Colombia: A two-year ambulatory study. Pediatrics 1983; 71: 210-8.
6. Weber M, Mulholland K, Greenwood B. Respiratory syncytial virus infection in tropical and developing countries. Trop Med and Internat Health 1998; 3: 268-80.
7. Holberg C, Wright A, Martinez F, et al. Risk factors for respiratory syncytial virus-associated lower respiratory illness in the first year of life. Am J Epidemiol 1991; 133: 1135-51.

โรคติดเชื้อทางเดินหายใจส่วนล่างจากเชื้อไวรัส เรสไปราตอรีย์ ซินซัยเทียล ในเด็กอายุต่ำกว่า 5 ปี ในพื้นที่ชนบทภาคกลางของประเทศไทย

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การศึกษาการป่วยด้วยโรคติดเชื้อทางเดินหายใจส่วนล่างจากเชื้อไวรัส เรสไปราตอรีย์ ซินซัยเทียล (RSV) ในเด็กอายุต่ำกว่า 5 ปี ได้ดำเนินการแบบ cohort study ที่อำเภอตาคลี จังหวัดนครสวรรค์ระหว่าง พฤศจิกายน 2541–กุมภาพันธ์ 2544 พบอุบัติการณ์ ในปีที่ 1 และปีที่ 2 เท่ากับ 12.6/1,000 child–year และ 5.8/1,000 child–year ตามลำดับ ในปีที่ 1 เชื้อ RSV เป็นสาเหตุของการป่วยด้วยโรคติดเชื้อทางเดินหายใจส่วนล่างเท่ากับร้อยละ 35.8 และลดลงในปีที่ 2 เป็นร้อยละ 17.5 ประมาณ 3 ใน 4 ของการติดเชื้อทางเดินหายใจส่วนล่างจากไวรัสนี้เกิดกับเด็กอายุต่ำกว่า 2 ปี ส่วนใหญ่ของการป่วยดังกล่าวทั้ง 2 ปี เกิดขึ้นระหว่างเดือน กรกฎาคมและตุลาคม ปัจจัยเสี่ยงของการป่วยคือ อายุต่ำกว่าหรือเท่ากับ 2 ปี (OR = 2.38, 95% CI = 1.22–4.67 p = 0.009) และนอนในห้องนอนเดียวกันกับสมาชิกอื่น ๆ เกิน 3 คน (OR = 2.92, 95% CI = 1.42–6.00, p = 0.002) ส่วนใหญ่ของการป่วยร้อยละ 63.9 จะได้รับการวินิจฉัยว่าเป็นปอดอักเสบ ไม่พบการเสียชีวิตจากการป่วย ในปีแรก RSV subtype B พบได้มาก ซึ่งตรงกันข้ามกับในปีที่ 2 ซึ่งพบเป็น subtype A เป็นส่วนใหญ่ เชื่อว่าการวิจัยที่มุ่งที่จะหาความสัมพันธ์ระหว่าง subtype ที่เฉพาะของ RSV และการเกิดความรุนแรงของโรค จะสามารถเป็นแนวทางในการพัฒนาวัคซีน สำหรับการป้องกันการเกิดการติดเชื้อจากไวรัสตัวนี้ได้ในอนาคต

คำสำคัญ : เชื้อไวรัส เรสไปราตอรีย์ ซินซัยเทียล, โรคติดเชื้อทางเดินหายใจส่วนล่าง

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